

### **REMARKS**

Claims 101-114 and 124-149 are pending in this application. Claims 130-149 have been added. Claims 101, 108, 124, and 127 have been amended. Support for the amendment to claim 101 can be found in the specification, e.g., at paragraph [059], and at paragraph [0194]. Support for the amendment to claim 108 can be found in the specification, e.g., at paragraph [0199]. Claims 124 and 127 have been amended by adding the word “or” before the last subpart of each claim. Support for new claim 130 can be found in the specification, e.g., at original claim 101 and at paragraph [0194]. Support for new claims 131-136 can be found in the specification, e.g., at original claims 102-107. Support for new claim 137 can be found in the specification, e.g., at original claim 108 and at paragraph [0199]. Support for new claims 138-143 can be found in the specification, e.g., at original claims 109-114. Support for new claims 144 and 147 can be found in the specification, e.g., at paragraphs [076] through [094]. Support for new claims 145 and 148 can be found in the specification, e.g., at paragraph [052]. Support for new claims 146 and 149 can be found in the specification, e.g., at paragraph [0102].

### **Objection**

The Examiner objected to claims 124 and 127, alleging that “the word ‘or’ is missing before the last compound of formula XI.” Action at page 2.

Solely to expedite prosecution and without acquiescing to the rejection, applicants have amended claims 124 and 127 by adding the word “or” before the last subpart in each of those claims.

Applicants respectfully request reconsideration and withdrawal of the objection to claims 124 and 127.

Rejection Under 35 U.S.C. § 102

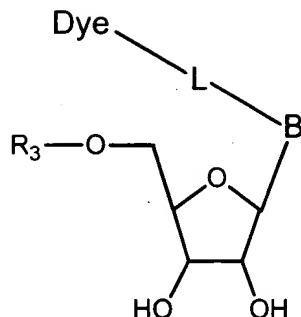
The Examiner rejected claims 101-113 and 124-129 under 35 U.S.C. 102(e) as allegedly being anticipated by U.S. Patent No. 6,500,650 (the '650 patent). Action at page 2. The Examiner alleged that

[t]he reference relates to a method for detecting polymorphism in a polynucleotide, comprising providing a polynucleotide suspected of containing a polymorphism; amplifying a segment of the polynucleotide encompassing the suspected polymorphism wherein amplification comprises replacing one or more natural nucleotide(s), one of which is a nucleotide involved in the suspected polymorphism, at substantially each point of occurrence in the segment with a modified nucleotide or, if more than one natural nucleotide is replaced, with different modified nucleotides to form an amplified modified segment; cleaving the amplified modified segment into fragments by contacting it with a reagent or reagents that cleave(s) the segment at substantially each point of occurrence of the modified nucleotide(s); hybridizing the fragments to an oligonucleotide; and, analyzing the hybridized fragments for an incorporated detectable label identifying the suspected polymorphism. (Summary of the invention).

Action at page 3 (emphasis added).

Applicants respectfully traverse. Applicants will address the rejection with respect to the claims cited by the Examiner, and also with respect to the claims added by this amendment. Solely to expedite prosecution and without acquiescing to the rejection, applicants have amended claims 101 and 108. Amended claim 101 recites:

101. A method for determining a polynucleotide sequence, comprising
  - (i) annealing at least one primer to a template polynucleotide;
  - (ii) extending said at least one primer in the presence of a mixture of at least four unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula:

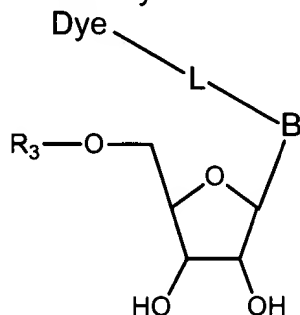


wherein B is a nucleobase; L is a linker; R<sub>3</sub> is triphosphate, α-thiotriphosphate, or a salt thereof, and Dye is a reporter group; so that primer extension products that contain at least one dye-labeled ribonucleotide are formed;

- (iii) cleaving one or more primer extension products to form a plurality of labeled fragments;
- (iv) separating the extension products by size; and
- (v) detecting the fragments to determine the polynucleotide sequence.

Claims 102-107 and 124-126 depend from claim 101. Amended claim 108 recites:

108. A method for detecting mutations in a polynucleotide, comprising
- annealing two primers to a template polynucleotide;
  - extending the two primers in the presence of a mixture of at least four unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula:



wherein B is a nucleobase; L is a linker; R<sub>3</sub> is triphosphate, α-thiotriphosphate, or a salt thereof, and Dye is a reporter group; so that primer extension products that contain at least one dye-labeled ribonucleotide are formed;

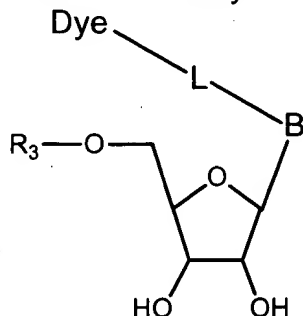
- cleaving one or more primer extension products to form a plurality of labeled fragments;
- separating the fragments by size; and
- detecting the fragments to detect the mutations.

Claims 109-114 and 127-129 depend from claim 108. Applicants have added claim

130, which recites:

130. A method for determining a polynucleotide sequence, comprising

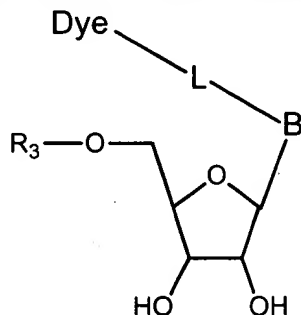
- (i) annealing at least one primer to a template polynucleotide;
- (ii) extending said at least one primer in the presence of a mixture of unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula:



- wherein B is a nucleobase; L is a linker; R<sub>3</sub> is triphosphate,  $\alpha$ -thiotriphosphate, or a salt thereof, and Dye is a reporter group;
- wherein at least one of the unlabeled dNTPs comprises a nucleobase that is the same as the nucleobase of at least one of the at least one dye-labeled ribonucleotide;
- so that primer extension products that contain at least one dye-labeled ribonucleotide are formed;
- (iii) cleaving one or more primer extension products to form a plurality of labeled fragments;
  - (iv) separating the extension products by size; and
  - (v) detecting the fragments to determine the polynucleotide sequence.

Claims 131-136 and 144-146 depend from claim 130. Applicants have also added claim 137, which recites:

137. A method for detecting mutations in a polynucleotide, comprising
- annealing two primers to a template polynucleotide;
  - extending the two primers in the presence of a mixture of unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula:



- wherein B is a nucleobase; L is a linker; R<sub>3</sub> is triphosphate,  $\alpha$ -thiotriphosphate, or a salt thereof, and Dye is a reporter group;
- wherein at least one of the unlabeled dNTPs comprises a nucleobase that is the same as the nucleobase of at least one of the at least one dye-labeled ribonucleotide;

so that primer extension products that contain at least one dye-labeled ribonucleotide are formed;

- cleaving one or more primer extension products to form a plurality of labeled fragments;

- separating the fragments by size; and

- detecting the fragments to detect the mutations.

Claims 138-143 and 147-149 depend from claim 137.

Applicants assert that the '650 patent does not teach "[a] method for determining a polynucleotide sequence comprising . . . extending said at least one primer in the presence of a mixture of at least four unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula . . . " as recited in claim 101. Applicants further assert that the '650 patent does not teach "[a] method for detecting mutations in a polynucleotide, comprising . . . extending the two primers in the presence of a mixture of at least four unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula . . . " as recited in claim 108. Applicants assert that the '650 patent does not teach "[a] method for determining a polynucleotide sequence comprising . . . extending said at least one primer in the presence of a mixture of unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula . . . wherein at least one of the unlabeled dNTPs comprises a nucleobase that is the same as the nucleobase of at least one of the at least one dye-labeled ribonucleotide," as recited in claim 130. Finally, applicants assert that the '650 patent does not teach "[a] method for detecting mutations in a polynucleotide, comprising . . . extending the two primers in the presence of a mixture of unlabeled dNTPs and at least one dye-labeled ribonucleotide having the formula . . . wherein at least one of the unlabeled dNTPs comprises a nucleobase that is the same as the nucleobase of at least one of the at least one dye-labeled ribonucleotide," as recited in claim 137.

Rather, the Examiner stated that the '650 patent discusses amplification comprising "replacing one or more natural nucleotide(s) . . . at substantially each point of occurrence in the segment with a modified nucleotide." Action at page 3. By "replacing one or more natural nucleotide(s) . . . at substantially each point of occurrence in the segment with a modified nucleotide" according to the '650 patent, applicants assert that the mixture cited by the Examiner would have fewer than four unlabeled dNTPs. Thus, the '650 patent does not teach a method in which the primer or primers are extended "in the presence of a mixture of at least four unlabeled dNTPs," as recited in claims 101 and 108. Furthermore, by "replacing one or more natural nucleotide(s) . . . at substantially each point of occurrence in the segment with a modified nucleotide," applicants further assert that the '650 patent does not teach a mixture "wherein at least one of the unlabeled dNTPs comprises a nucleobase that is the same as the nucleobase of at least one of the at least one dye-labeled ribonucleotide."

For at least those reasons, applicants assert that the '650 patent does not anticipate any of claims 101, 108, 130, and 137. Furthermore, for at least those reasons, the '650 patent also does not anticipate any of dependent claims 102-107, 124-129, 131-136, and 138-149. Because the '650 patent fails to teach all of the elements of independent claims 101, 108, 130, and 137, applicants need not address the Examiner's contention concerning certain limitations of certain dependent claims. By not addressing those contentions, applicants in no way acquiesce to those contentions.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e) over the '650 patent.

Applicants respectfully assert that the present application is in condition for allowance and request that the Examiner issue a timely Notice of Allowance. If the Examiner does not find the application allowable, the undersigned requests that, prior to taking action, the Examiner call her at (650) 849-6656 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Dated: July 1, 2004

By: 

Rebecca B. Scarr  
Reg. No. 47,057  
Customer No. 22,852